REMARKS

Continued Examination, pursuant to 37 C.F.R. § 1.114, is requested on the basis of the Amendment and accompanying remarks filed April 5, 2011. In particular response to the Examiner's remarks appended to the Advisory Action dated April 25, 2011, Applicants provide the following supplemental reply:

Regarding the claims which read on the species elected for examination.

In remarks which continue item 3 of the Advisory Action, the Examiner has asserted that Applicants have failed to provide a list of claims believed to read upon the elected species.

In the Reply filed December 22, 2009, applicants indicated election of Group I, and further provided election of election of a species of:

- phosphatidylcholine from among the phospholipids disclosed on pages 14-15,
- polyethylene glycol, from among the hydrophilic molecules disclosed on pages 14-15 and
- doxorubicin hydrochloride from among the drugs disclosed on pages 29-31 of the specification.

In electing Group I and the various species, Applicants noted the election of Claims 1-17 which were believed to correspond to the invention of Group I and to be generic to the various elected species. In the Office Action dated April 19, 2010, the Examiner contended that claims 7-9 and 13 did not read upon the elected species. However, while Applicants did not agree with that determination, the issue would be moot if, as Applicants maintain, generic claims are allowable.

In the amendment filed April 5, 2011, a portion of the subject matter of claim 13 has been incorporated into claim 1. With respect to claim 13, the election of polyethylene glycol, from among the hydrophilic macromolecules disclosed on pages 14-15 did not define the manner in which the hydrophilic macromolecule is introduced into the liposome preparation. Two of the ways in which any hydrophilic macromolecule can be introduced into the

liposome preparation of claim 1 were recited in former claim 13. Therefore, claim 13 would have read upon any hydrophilic macromolecule introduced as recited in claim 13 and was generic to the elected hydrophilic macromolecule. Accordingly, claim 1 as amended continues to fall within the scope of the elected invention.

Moreover, as the Examiner has reiterated the request for further elaboration on the subject of claims reading on the elected species, Applicant's representative notes the following:

With respect to claim 8, the election of phosphatidylcholine lipids as the main membrane component recited in claim 1 does not exclude that the liposome may comprise another lipid in addition to the main membrane component as recited in claim 8. The same is true for claim 9, which recites that the lipid bilayer may further comprise cholesterol in addition to the elected main membrane component.

Thus, contrary to the Examiner's determination, at least claims 8, 9 and 13 are generic to the elected species. However, applicants continue to expect the issue to be moot in view of the patentability of generic claims.

Regarding the patentability of the amended claims over the cited art.

In remarks which continue item 11 of the Advisory Action, the Examiner has asserted that the prior art teaches each of the individual elements of the claimed invention.

Applicants respectfully point out that an invention composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. *KSR Int'l Co. v. Teleflex Inc.*, 550 US 398, 418, 82 U.S.P.Q.2d 1385, 1388 (2007). To make out a prima facie case requires a rational supported by sound scientific reasoning for modifying the prior art to arrive at the claimed combination arranged as required by the claim.

The Examiner has further contended that the reasons for putting PEG on the exterior of a liposome are considered to be readily evident to one of ordinary skill in the art. However, that is not all that is required by the claims. Claim 1 recites a unilamellar vesicle

comprising an interior aqueous phase at a pH of up to 5 with a drug loaded therein, and wherein the unilamellar vesicle is modified with a hydrophilic macromolecule only on its exterior surface and the hydrophilic macromolecule is introduced as a phospholipid derivative of the hydrophilic macromolecule.

Neither Mayer nor Harigai suggested a liposome preparation comprising all the features of claim 1. Neither Mayer nor Harigai suggested that the problem of liposome stability for drugs which must be maintained at low pH could be solved by including a hydrophilic macromolecule only on the exterior liposome surface of a unilamellar vesicle. Indeed, Mayer proposed distinctly different approaches to providing for long term storage. See, e.g. col. 16-17. The surprising stability of liposomes having the features recited in the claims -- without resort to the methods of Mayer – is demonstrated by the examples of the specification. There is no evidence that the prior art appreciated the solution provided by the present invention, which is therefore, objectively demonstrated to be non-obvious.

Thus, for the reasons which have been previously stated, the claims are believed to be patentable over the cited art.

Respectfully submitted,

BUCHANAN INGERSOLL & ROONEY PC

Date: May 5, 2011

By: /Christopher L. North/
Christopher L. North
Registration No. 50433

Customer No. 21839
703 836 6620